ADAPTATION OF MUSCLE DURING SEVERE CHRONIC HYPOXIA

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Chronic exposure to hypoxia of humans during long-term high altitude residence causes considerable reductions in body and skeletal muscle mass as well as a reduction in the muscle mitochondrial density¹. In contrast to mammals, fish seem to be able to move actively and increase body mass under severe chronic hypoxia². This raises the question how fish skeletal muscle adapts to chronic hypoxia. The aim of this study was to investigate the mechanisms underlying the adaptation of muscle fibre size and oxidative capacity of zebrafish muscle during long-term adaptation to chronic hypoxia. For high and low oxidative muscle fibres, we investigated changes in muscle fibre cross-section area (CSA), mitochondrial density, capillarisation, myonuclear density and myoglobin protein as well as mRNA expression during chronic hypoxia.

Zebrafish (Danio rerio) were kept in aquaria (28 °C) for 3 or 6 weeks at 10% air saturation (hypoxia) or at 90% air-saturation (normoxia). After these periods, fish were frozen in liquid nitrogen and cross-sections were cut from the tail using a cryostat. Calibrated histochemistry was used to determine succinate dehydrogenase activity³ (SDH, a measure of VO₂max) and myoglobin concentration⁴,⁵.

After three weeks of hypoxia, both high and low oxidative fibres did not show differences in CSA, SDH activity, myoglobin concentration, capillary and myonuclear density between normoxic and hypoxic conditions. Myoglobin mRNA staining of hypoxic high oxidative muscle fibres was 53% higher than of normoxic fibres. After six weeks of hypoxia for both high and low oxidative muscle fibres, CSA, capillary and myonuclear density were still not changed. However, high oxidative muscle fibres showed an increase in SDH activity and myoglobin concentration of 54% and 42%, respectively, compared to the six weeks normoxic high oxidative muscle fibres. Staining intensity of myoglobin mRNA in hypoxic high oxidative muscles was 52% higher than control. In low oxidative muscle fibres SDH activity as well as myoglobin protein and mRNA concentrations were unchanged.

We conclude that high oxidative skeletal muscle fibres of zebrafish enhance the oxidative capacity during chronic hypoxia. Oxygen supply to mitochondria is facilitated by an increased myoglobin concentration, which is regulated by an elevated myoglobin mRNA content per myonucleus. These results indicate that fish and human skeletal muscle fibres adapt in opposite directions to chronic hypoxia.


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